REMARKS

Further consideration of the application as amended is respectfully requested. Claims 94-95 and 99-106 are currently pending and have been allowed by the Examiner. The claims have been amended by adding new claims 107-129. The new claims are fully supported by the specification and claims as originally filed and present no new matter.

Claim 107 recites a vaccine comprising an isolated PMPE polypeptide of a *Chlamydia spp.* comprising an amino acid sequence of SED ID No.: 2. Support is found throughout the specification in particular at sections 3, 5.1, 5.3, 5.4, 5.6, and 5.7 and original claims 15, 29, 31 and 32.

Claims 108, 109 and 110 recite vaccines comprising homologs and antigenic fragments of the PMPE polypeptide of SEQ ID No.: 2. Claims 128 and 129 are drawn to immunogenic compositions comprising homologs and antigenic fragments of the PMPE polypeptide of SEQ ID No.: 2. Support is found throughout the specification. The specification discloses two full length PMPE polypeptides, SEQ ID No.: 2 and the PMPE protein encoded by the plasmid contained within ATCC deposit PTA-2462. See specification page 58. Reference in the specification to a deposit in a public depository constitutes an adequate written description for purposes of section 112, first paragraph. See *Enzo Biochem v Gen-Probe*, 323 F3d 956, 965 (Fed Cir 2002), reversing its earlier decision in *Enzo Biochem v Gen-Probe*, 285 F3d 1013 (Fed Cir 2002).

The specification clearly teaches how to make and use vaccines and immunogenic compositions comprised of fragments of the claimed PMPE polypeptides at sections 5.1, 5.2, 5.3, 5.4 and 5.7. The specification teaches an assay to determine if a particular peptide or analog is efficacious in inducing an immunoprotective response at section 6.9.2, pages 64-65. The specification teaches how to make and use such fragments using recombinant expression at section 5.5.

Claim 116 recites a vaccine polypeptide produced by culturing a host cell containing plasmid M15 pREP (pQE-pmpE-Ct)#37 obtainable from *E. coli* having ATCC accession No. PTA-2462 and recovering said polypeptide. Support is found in sections 5.1, 5.7, 6 and in particular 6.11.

Claims 111, 112, 114, 114, 115 and 117 recite vaccines produced by culturing a host cell with nucleic acids encoding PMPE polypeptides. Support is found throughout the specification, in particular sections 6.11, 6.13 and 6.15.

Claims 118-127 are dependent claims supported throughout the specification.

Rejections under 35 USC 112 first paragraph

Applicant respectfully submits that vaccines of the amended claims comprised of homologs and fragments of *Chlamydia* PMPE polypeptides are adequately described. Claims are drawn to polypeptides of SEQ ID No.: 2 or its close homologs or antigenic fragments. One such homolog is described in the plasmid of ATCC No. PTA-2462. As previously explained in response to office action filed November 5, 2002, page 11, the

homolog sequences differ at eight specific amino acid residues. The specification teaches allelic variants of the PMPE polypeptide at pages 19 and 20. An allelic variant with at least 90% sequence homology is exemplified in the plasmid of ATCC No. PTA-2462. The specification fully describes homologs with at least 90% sequence identity.

More importantly, and more emphatically, Applicant restates arguments concerning the adequacy of written description of antigenic fragments of the PMPE polypeptides. The specification discusses antigenic fragments of the fully disclosed PMPE of SEQ ID No.: 2 at great length. Numerous specific fragments are disclosed, including SEQ ID Nos.: 4, 5, 6, 7, 8, 9, 10 and 11. The specification clearly teaches at 5.1, 5.2, 5.3, 5.4 and 5.7 how to make and use vaccines and immunogenic compositions comprised of fragments of the claimed PMPE polypeptide of SEQ ID No.: 2. The specification also teaches an assay to determine if a particular peptide or analog is efficacious in inducing an immunoprotective response at section 6.9.2, pages 64-65. The specification teaches how to make and use such fragments using recombinant expression at section 5.5.

Applicant respectfully submits that the written description requirement for antigenic fragments is fully satisfied and, moreover, that such fragments have been fully enabled. As previously argued, and as previously supported by cited references that were not considered in the Office Action of February 12, 2003, epitope scanning is a common technique, well known and routinely practiced by those with ordinary skill in the art. Here Applicant has resubmitted the previously cited references in an effort to

demonstrate, once again, that epitope scanning is routine practice. See *Deslauriers et al* , Infection and Immunity 64:434 (1996), and *Sexton et al*, J. Immunology, 152:1861 (1994), and *Briles et al*, US Patent #5,965,141, and *Carlson et al*, Infection and Immunity, 65:2080 (1997), and *Nilsson et al*, C. Clin. Invest., 101:2640 (1998), and *Charles et al*, US Patent #5, 976, 544. Applicant respectfully notes that the Board of Patent Appeals and Interferences has generally agreed with the applicant concerning the routine practice of epitope scanning. See e.g. *Ex Parte Yuji Noguchi,* Appeal No. 1999-1422, BPAI, application no. 08/408,915.

Rejections under 36 USC 112 second paragraph

Claims drawn to vaccines produced by recombinant expression, formerly numbered claims 91-93, were rejected as indefinite for use of the phrase "under conditions suitable for expression of said PMPE polypeptide." The specification clearly teaches how to recover expressed recombinant PMPE polypeptides using a variety of techniques well known to those of ordinary skill in the art. See specification, section 6.11, 6.12, 6.13, and 6.15. A applicant has deleted the phrase "under conditions suitable for expression of said PMPE polypeptide" from the claims, in order that the claims be clarified.

Rejections under 35 USC 102

Claims to vaccines comprised of the full length *Chlamydia* PMPE polypeptide and its antigenic fragments and claims to vaccines produced by recombinant expression of *Chlamydia* PMPE polypeptides were rejected as anticipated by *Griffais et al*, WO 99/28474 and by *Probst et al* in both US Patent #6,432,916 and WO 00/34483.

Both *Probst* SEQ ID No.: 177 and *Griffais* SEQ ID No.: 31 are disclosed as "vaccines." These amino acid sequences have greater than 98% sequence identity with the *Chlamydia* PMPE polypeptide disclosed here as SEQ ID No.: 2.

Applicant respectfully submits that neither *Probst* nor *Griffais* can anticipate the present invention, because neither *Probst* nor *Griffais* enabled a PMPE vaccine. In order for a reference to anticipate, it must teach and enable each element of the claimed invention. *Griffais* makes a purely bioinformatic disclosure, claiming as a "vaccine" each and every theoretical ORF of an entire *Chlamydia* genome – some 1197 "vaccines" in all. *Probst* provides slightly more information in support of "vaccine" claims, but falls far short of enabling any, save, arguably, the very narrow claims that were actually allowed in US Patent 6,432,916 – claims to a recombinant N-terminal sequence from a putative cap1 gene product which was localized to *Chlamydia* inclusion membranes, not elementary bodies.

Those of ordinary skill in the art would have no reasonable expectation of success using any one of the 293 theoretical "vaccines" disclosed by *Probst* or the 1197 theoretical "vaccines" disclosed by *Griffais*.

Of the nine pmp genes identifiable in genomes of various strains of *Chlamydia*

trachomatis, only three are actually expressed at the outer member surface at levels sufficient to render these antigens immunodominant (pmpE, pmpG, pmpH). See *Stothard et al*, Infection and Immunity, 71:1200 (2003), and *Tanzer et al*, J. Bacteriology, 183:2686 (2001), and *Mygind et al*, FEMS Microbiol Lett, 186:163 (2000). Similarly, with *Chlamydia pneumoniae*, only 8 of 21 identifiable, theoretical pmp/omp proteins are actually expressed at the outer member surface at levels sufficient to render these antigens immunodominant. See *Grimwood et al*, Infection and Immunity, 69:2383 (2001) and *Christiansen et al*, J. Infectious Diseases, 181:S528 (2000).

Neither *Griffais* nor *Probst* isolate, much less, test a *Chlamydia* pmp polypeptide *in vitro*, much less, *in vivo*. *Griffais* discloses as "vaccines" all nine *Chlamydia* pmp ORFs, while *Probst* attempts to claim, as "vaccines," 6 theoretical pmps identified as SEQ ID Nos.: 176-181 including only 2 that are actually expressed at appreciable levels (pmpE and pmpG). With respect to *Chlamydia* pmp "vaccines," one skilled in the art would have at the very best 1 chance in 3 of being able to practice the invention of *Probst* or *Griffais*, since only 1 in 3 of the claimed pmp polypeptides are actually expressed on the outer membranes surface at meaningful levels.

Applicant respectfully submits that, in the case of both *Griffais* and *Probst*, the disclosed "vaccines" are analogous to "mere naming" in chemical patents – *Griffais* presents no data whatsoever concerning any of 1197 theoretical "vaccines." *Probst* presents some data *in vitro*. See Example 2, Example 5, Example 7, Example 8. However, *Probst* data *in vitro* tend only to diminish any inference that 293 theoretical

"vaccines" would actually work. Of all the "vaccines" disclosed, only two were tested, *in vivo*, and only one actually worked. Ironically, one of these two promising prospective antigens, the S13 ribosomal protein, was prominently featured by *Probst* as an antigen in the disclosure. Indeed, *Probst* claims to have isolated its epitopes. Fig 7a, Fig 8, Col 51 L 45-60. Yet *in vivo*, S13 was *not* immunoprotective. Col 68, L 8-37.

With respect to recombinant polypeptides, even where a native pmp protein is, itself, highly expressed and immunodominant, the recombinant protein can fail to prove immunoprotective, because its epitopes are conformational. Especially with membrane proteins, recombinant proteins may be non-natively folded so as to be non-immunoprotective. See e.g. *Christiansen et al*, J. Infectious Diseases, 181:S528 (2000)[recombinant OMP peptides from *Chlamydia pneumoniae* did not react with human sera that apparently recognized native OMP peptides]. And see *Hou et al*, Infection and Immunity, 71:6844 (2003) and *Exner et al*, Infection and Immunity, 68:2647 (2000).

It is well known to those skilled in the art that antigenicity *in vitro* does not predetermine immunoprotection *in vivo*. There is such unpredictability in the art of vaccines that even the most promising theoretical antigens are commonly referred to only as vaccine "candidates." Indeed, it is because of this unpredictability that the PTO holds vaccine claims to a heightened standard of enablement. Applicant respectfully submits that *Probst* and *Griffais*, having presented no evidence of PMPE antigenicity and immunoprotection, cannot anticipate the present invention.

Rejections under 35 USC 103

Claims to vaccines comprised of the full length *Chlamydia* PMPE polypeptide and its antigenic fragments were rejected as obvious over *Probst et al* US Patent #6,432,916 in light of *Murdin et al*, Infection and Immunity, October 1992, p. 4406.

Applicant respectfully submits that, at best, the Examiner has presented a case of obvious to try, as a candidate antigen, a theoretical outer membrane protein from *Chlamydia trachomatis* in combination with the poliovirus-chlamydia hybrid vaccine disclosed by *Murdin et al*. This does not make a case of *prima facie* obviousness. As explained above, one skilled in the art had no reasonable expectation of success that any one theoretical, recombinant, outer membrane candidate antigen would prove immunoprotective *in vivo*. The art itself is highly unpredictable. Moreover, only one in three such theoretical proteins are actually expressed in the outer membrane at appreciable levels.

CONCLUSION

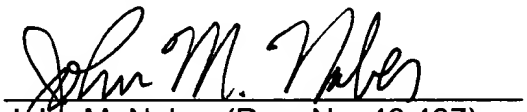
Accordingly, in light of the above remarks and references, Applicant respectfully submits that new claims 107 through 129 are patentable for the reasons set forth above. Applicant respectfully requests all rejections be withdrawn, and that all claims pending be allowed.

In light of the foregoing, Applicant respectfully submits that each item set forth in the Office Action dated February 12, 2003 has been addressed. Further, Applicant submits that all claims are now in condition for allowance and respectfully requests such allowance.

In the event any further matters requiring attention are noted by the Examiner or in the event that prosecution of this application can otherwise be advanced thereby, a telephone call to Applicant's undersigned representative at the number shown below is invited.

Respectfully submitted,

Dated: May 25, 2005

By: 

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